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Assembly of Substituted 3-Aminoindazoles from 2-Bromobenzonitrile via a CuBr-Catalyzed Coupling/Condensation Cascade Process

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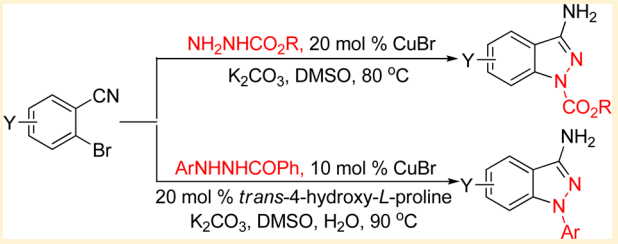
Supporting Information

ABSTRACT: CuBr-catalyzed coupling reaction of 2-halobenzonitriles with hydrazine carboxylic esters and CuBr/4-hydroxy-L-proline-catalyzed coupling reaction of 2-bromobenzonitriles with *N*′-arylbenzohydrazides proceed smoothly at 60−90 °C to provide substituted 3-aminoindazoles through a cascade coupling/condensation (or coupling/deacylation/condensation) process. A wide range of 3-aminoindazoles with substituents at both the 1-position and the phenyl ring part can be prepared from the corresponding coupling partners.



3-Aminoindazole is a medicinally important heterocyclic moiety that has been frequently applied for pharmaceutical design. The compounds with this special skeleton have been demonstrated to have significant biological activities, ranging from blocking melanin-concentrating hormone (MCH) receptor-1 as displayed by compounds **1** and **2** (Figure 1)[1] to inhibiting multitargeted receptor tyrosine kinase (RTK), janus kinase 2 (JAK-2), and cyclin-dependent kinase as shown by ABT-869 (**3**),[2] compounds **4**[3] and **5**,[4] respectively.

The typical method for assembling 3-aminoindazoles has relied on an aromatic nucleophilic substitution of *o*-fluorobenzonitriles and *o*-chlorobenzonitriles with hydrazine.[1−5] The major drawback for this approach is that when electron-rich *o*-halobenzonitriles were used harsh reaction conditions were required and the reactions normally gave the desired products in low yields. This problem is believed to result from the deactivation directed by the additional electron-donating groups. Additionally, in order to obtain 1-substituted 3-aminoindazoles, further functionalization at the 1-position of its products was required. Other notable synthetic methods included condensation of N-substituted fluoroarythioamides with hydrazine,[6] Pd-catalyzed amination of 3-chloroindazoles,[7] and Pd-catalyzed intramolecular C−N bond formation of tosylhydrazines.[8] These approaches suffer from requiring several steps to obtain the starting materials. Recently, Fabis and co-workers reported that 3-aminoindazoles could be obtained by Pd-catalyzed arylation of benzophenone hydrazine with substituted 2-bromobenzonitriles and subsequent deprotection and intramolecular condensation.[9] Since this method needs both basic and acidic operations at relatively high temperatures, its applications for diverse synthesis are questionable.

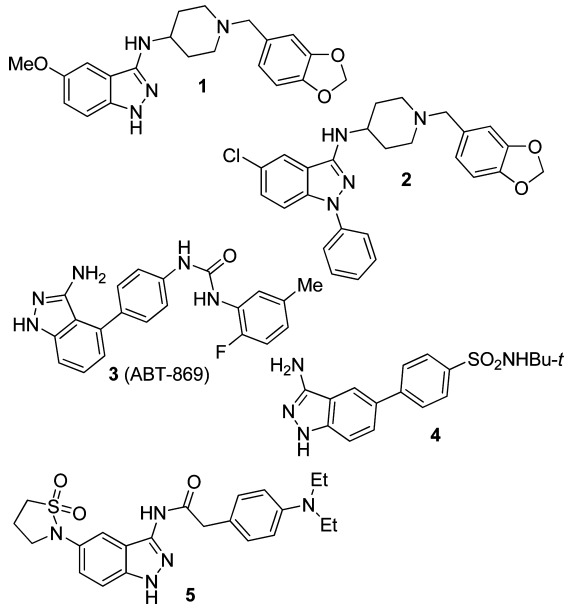


Figure 1. Selected bioactive compounds with 3-aminoindazole moiety.

During the past decade, arylation of hydrazine or its derivatives under the catalysis of metal complexes has received great attention.[9−12] Based on our investigations on Cu-

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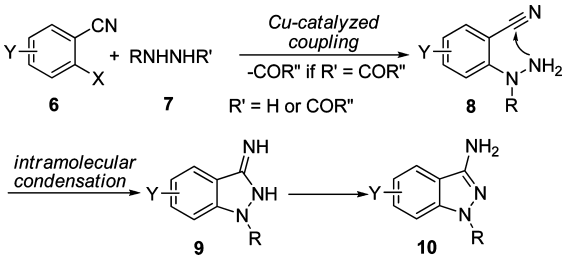
catalyzed coupling of aryl halides with protected hydrazines,[10] we speculated that Cu-catalyzed coupling of 2-halobenzonitriles **6** with protected hydrazines **7** might occur regioselectively to afford aryl hydrazines **8** directly or after deacylation (Scheme 1). The resultant intermediates **8** could undergo spontaneous

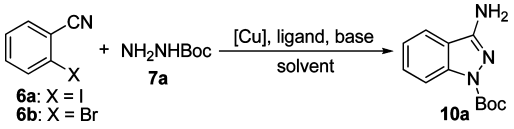
Scheme 1



intramolecular condensation to afford cyclization products **9**, which would deliver 1-substituted 3-aminoindazoles **10** after aromatization.

With this idea in mind, we conducted a coupling reaction of 2-iodobenzonitrile with *N*-Boc-hydrazine. It was found that under the catalysis of 20 mol % of CuI and 20 mol % of L-proline, the reaction proceeded smoothly in DMF at room temperature to afford the desired *tert*-butyl 3-amino-1*H*-indazole-1-carboxylate **10a** in 68% yield (Table 1, entry 1).

Table 1. Condition Screening for Formation of *tert*-Butyl 3-Amino-1*H*-indazole-1-carboxylate 10a[a]



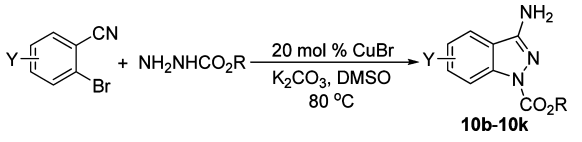
entry	X	[Cu]	solvent	temp (°C)	time (h)	yield[b] (%)
1	I	CuI	DMF	rt	56	68[c]
2	I	CuI	DMF	rt	56	86
3	I	CuI	1,4-dioxane	rt	56	41
4	I	CuI	DMSO	rt	40	85
5	Br	CuI	DMF	80	24	27
6	Br	CuCl	DMF	80	12	14
7	Br	Cu_2O	DMF	80	12	35
8	Br	CuBr	DMF	80	12	60
9	Br	CuBr	DMSO	80	12	77

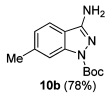
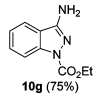
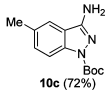
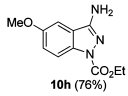
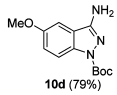
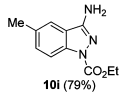
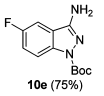
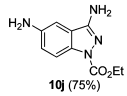
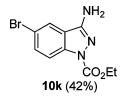
[a]Reaction conditions: 2-halobenzonitrile (0.5 mmol), hydrazine carbamate (0.6 mmol), copper salt (0.1 mmol), K_2CO_3 (1 mmol). [b]Isolated yield. [c]L-Proline as the additive.

In the absence of L-proline a better yield was observed (entry 2), indicating that the ligand is useless in this case. A similar phenomenon has been observed in our studies on simple arylation of *N*-Boc-hydrazine.[10a] For other solvents, 1,4-dioxane gave a lower yield (entry 3), while DMSO led to complete conversion in a shorter time (compare entries 2 and 4). When less reactive 2-bromobenzonitrile was used, the cascade reaction process worked in DMF at 80 °C, although the yield was poor (entry 5). The condition screening by changing copper salts revealed that CuBr is a more efficient catalyst (compare entries 5−8). The reaction yield could be further improved by using DMSO as the solvent (entry 9). Taken together, we concluded that using CuBr as the catalyst and DMSO as the solvent could give the best results.

We next examined the reaction scope by varying 2-bromobenzonitriles and protected hydrazines. As summarized in Table 2, three electron-rich and one electron-deficient 2-

Table 2. Synthesis of 3-Aminoindazoles via a CuBr-Catalyzed Cascade Reaction Process from Hydrazine Carboxylic Esters and 2-Bromobenzonitriles[a]



entry	product (yield)	entry	product (yield)
1	 **10b** (78%)	6	 **10g** (75%)
2	 **10c** (72%)	7	 **10h** (76%)
3	 **10d** (79%)	8	 **10i** (79%)
4	 **10e** (75%)	9	 **10j** (75%)
5[c]	 **10f** (65%)	10[c]	 **10k** (42%)

[a]Reaction conditions: 2-bromobenzonitrile (0.5 mmol), hydrazine carbamate (0.6 mmol), CuBr (0.1 mmol), K_2CO_3 (1 mmol), 80 °C, 12 h. [b]Isolated yield. [c]Reaction was carried out at 60 °C.

bromobenzonitriles also worked well, affording the corresponding 3-aminoindazoles **10b−e** in good yields (entries 1−4). These results indicated that the electronic nature of 2-bromobenzonitriles has little influence to the present transformation.

Further investigations revealed that changing Boc to other protecting groups was possible, evident because 3-aminoindazoles **10f−k** could be obtained from the corresponding 2-bromobenzonitriles and hydrazine carboxylic esters (entries 5−10). Obviously, compounds **10d**, **10j**, and **10k** could be used for preparing melanin-concentrating hormone (MCH) receptor antagonist **1**,[1] cyclin-dependent kinase inhibitor **5**,[4] multi-targeted receptor tyrosine kinase (RTK) inhibitor **3**,[2] and janus kinase 2 (JAK-2) inhibitor **4**,[2] respectively.

We have recently found that *N*-acyl-*N*′-arylhydrazines could couple with aryl iodides regioselectively to afford *N*-acyl-*N*′,*N*′-diarylhydrazines under the catalysis of CuI and 4-hydroxy-L-proline.[10b] We speculated that these nucleophiles could react with 2-bromobenzonitriles to give the coupling products, which would undergo deacylation and intramolecular condensation to deliver aryl-substituted 3-aminoindazoles. Accordingly, CuBr/4-hydroxy-L-proline-catalyzed coupling of 2-bromobenzonitrile and *N*′-phenylbenzohydrazide was conducted. We were pleased that the reaction took place at 90 °C to provide 1-phenyl-3-aminoindazole **10l** in 82% yield (Table 3, entry 1). Using *N*′-phenylbenzohydrazide as a coupling partner, some substituted 2-bromobenzonitriles were checked and good yields were observed for both electron-rich and electron-deficient sub-

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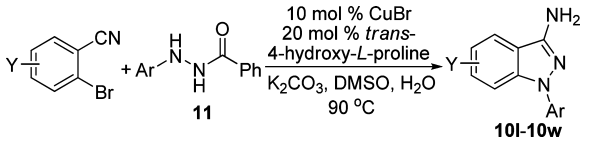
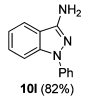
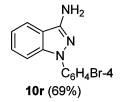
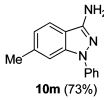
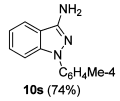
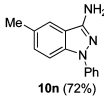
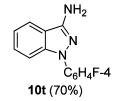
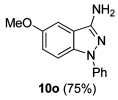
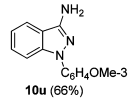
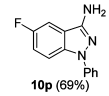
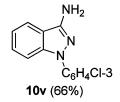
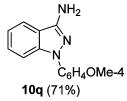
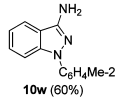
Table 3. Synthesis of 3-Aminoindazoles from 2-Bromobenzonitriles and *N*′-Arylbenzohydrazides under the Catalysis of CuBr and *trans*-4-Hydroxy-L-proline[a]



entry	product (yield)	entry	product (yield)
1	 **10l** (82%)	7	 **10r** (69%)
2	 **10m** (73%)	8	 **10s** (74%)
3	 **10n** (72%)	9	 **10t** (70%)
4	 **10o** (75%)	10	 **10u** (66%)
5	 **10p** (69%)	11	 **10v** (66%)
6	 **10q** (71%)	12	 **10w** (60%)

[a]Reaction conditions: 2-bromobenzonitrile (0.5 mmol), *N*′-arylbenzohydrazide (0.6 mmol), CuBr (0.05 mmol), *trans*-4-hydroxy-L-proline (0.1 mmol), K_2CO_3 (2 mmol), DMSO (1.5 mL), H_2O (0.15 mL), 90 °C, 48 h. [b]Isolated yield.

strates (entries 2−5). Further attempts indicated that a wide range of aryl groups could be introduced to the 1-position of 3-aminoindazoles by employing different *N*′-arylbenzohydrazides as the coupling partners (entries 6−12). No regioisomers of **10l−w** were determined from these reactions, indicating that the first coupling step took place in a regioselective manner as we observed before.[10b] Noteworthy is that without addition of 4-hydroxy-L-proline the reaction yield decreased greatly.

It is notable that using *N*-acyl-*N*′-arylhydrazines as the coupling partners is essential for this transformation because coupling of phenyl hydrazine with 2-bromobenzonitrile under similar conditions (CuBr/*trans*-4-hydroxy-L-proline, K_2CO_3, DMSO, 100 °C) did not give any coupling products. These results demonstrated that subtle change in pK_a values of nucleophiles could alter the coupling reaction process greatly.

In conclusion, we have developed a valuable method for assembling pharmaceutically important substituted 3-aminoindazoles. This method relies on a copper-catalyzed coupling reaction of 2-halobenzonitriles with hydrazine carboxylic esters and *N*′-arylbenzohydrazides. Its generality has been demonstrated by synthesizing a number of 3-aminoindazoles with substituents at both the 1-position and the phenyl ring part. Our result gives another example for illustrating the usage of copper-catalyzed coupling in heterocycles synthesis.[13,14]

EXPERIMENTAL SECTION

General Procedure for Synthesis of 3-Aminoindazoles. A Schlenk tube was charged with 2-iodobenzonitrile (0.5 mmol), hydrazines (0.6 mmol), CuBr (0.1 mmol), and K_2CO_3 (1.0 mmol). The tube was evacuated and backfilled with argon before 1.0 mL of DMSO was added. The reaction mixture was stirred at 80 °C (60 °C for benzyl hydrazinecarboxylate) for 10−24 h. After the reaction mixture was cooled, 10 mL of saturated NH_4Cl was added. The mixture was extracted with EtOAc, and then the organic layer was washed with water and brine and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by column chromatography on silica gel (eluting with Et_3N/EtOAc/hexane) to provide the desired product.

*tert-Butyl 3-amino-1H-indazole-1-carboxylate (**10a**):* white solid, 88 mg, 77% yield; mp 157−159 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.58 (s, 9H), 6.33 (br s, 2H), 7.26 (t, J = 7.6 Hz, 1H), 7.51 (dt, J = 0.8, 7.2 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.4, 149.2, 139.9, 129.1, 122.5, 120.7, 119.3, 114.1, 82.4, 27.9; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{12}H_{15}N_3NaO_2$ 256.1062, found 256.1063.

*tert-Butyl 3-amino-6-methyl-1H-indazole-1-carboxylate (**10b**):* white solid, 95 mg, 78% yield; mp 140−142 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.57 (s, 9H), 2.44 (s, 3H), 6.25 (br s, 2H), 7.10 (d, J = 8.8 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.3, 149.2, 140.5, 139.1, 124.0, 120.3, 117.3, 114.1, 82.2, 27.9, 21.7; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{13}H_{17}N_3NaO_2$ 270.1219, found 270.1215.

*tert-Butyl 3-amino-5-methyl-1H-indazole-1-carboxylate (**10c**):* white solid, 88 mg, 72% yield; mp 164−166 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.57 (s, 9H), 2.39 (s, 3H), 6.25 (br s, 2H), 7.33 (d, J = 8.4 Hz, 1H), 7.62 (s, 1H), 7.83 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.2, 149.1, 138.3, 131.6, 130.4, 120.1, 119.5, 113.80, 82.1, 27.9, 20.7; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{13}H_{17}N_3NaO_2$ 270.1219, found 270.1215.

*tert-Butyl 3-amino-5-methoxy-1H-indazole-1-carboxylate (**10d**):* semisolid, 102 mg, 79% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.57 (s, 9H), 3.80 (s, 3H), 6.24 (br s, 2H), 7.14 (dd, J = 2.0, 8.8 Hz, 1H), 7.40 (d, J = 2.0 Hz, 1H), 7.84 (d, J = 9.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.3, 152.3, 149.1, 134.9, 119.9, 118.6, 115.0, 102.2, 82.1, 55.5, 27.9; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{13}H_{17}N_3NaO_3$ 286.1168, found 286.1163.

*tert-Butyl 3-amino-5-fluoro-1H-indazole-1-carboxylate (**10e**):* white solid, 94 mg, 75% yield; mp 142−144 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.57 (s, 9H), 6.34 (s, 2H), 7.38 (td, J = 9.1, 2.6 Hz, 1H), 7.66 (dd, J = 8.5, 2.5 Hz, 1H), 7.96−7.93 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 159.0 (J = 237.1 Hz), 152.1, 149.0, 136.7, 119.9 (J = 9.5 Hz), 117.5 (J = 25.5 Hz), 115.6 (J = 9.1 Hz), 106.1 (J = 24.3 Hz), 82.6, 27.9; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{12}H_{14}FN_3NaO_2$ 274.0968, found 274.0975.

*Benzyl 3-amino-1H-indazole-1-carboxylate (**10f**):* white solid, 86 mg, 65% yield; mp 175−177 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.39 (s, 2H), 6.41 (br s, 2H), 7.27−7.55 (m, 7H), 7.88 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.9, 150.2, 139.9,135.8, 129.3, 128.5, 128.4, 128.3, 122.8, 120.8, 119.5, 113.9, 67.6; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{15}H_{13}N_3NaO_2$ 290.0906, found 290.0895.

*Benzyl 3-amino-1H-indazole-1-carboxylate (**10g**):* white solid, 76 mg, 75% yield; mp 164−165 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.34 (t, J = 6.8 Hz, 3H), 4.37 (q, J = 6.8 Hz, 2H), 6.39 (br s, 2H), 7.28 (t, J = 7.6 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.88 (d, J = 8.0 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.8, 150.4, 139.9, 129.2, 122.7, 120.8, 119.4, 113.9, 62.4, 14.3; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{10}H_{11}N_3NaO_2$ 228.0749, found 228.0757.

*Ethyl 3-amino-5-methoxy-1H-indazole-1-carboxylate (**10h**):* white solid, 89 mg, 76% yield; mp 176−178 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.33 (t, J = 6.8 Hz, 3H), 3.80 (s, 3H), 4.34 (q, J = 6.8 Hz, 2H), 6.28 (br s, 2H), 7.15 (dd, J = 1.6, 8.4 Hz, 1H), 7.41 (s, 1H), 7.88 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ

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155.5, 152.6, 150.3, 134.9, 120.0, 118.7, 114.8, 102.3, 62.2, 55.5, 14.3; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{11}H_{13}N_3NaO_3$ 258.0855, found 258.0847.

*Ethyl 3-amino-5-methyl-1H-indazole-1-carboxylate (**10i**):* white solid, 86 mg, 79% yield; mp 143−145 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.33 (t, J = 6.8 Hz, 3H), 2.40 (s, 3H), 4.33 (q, J = 6.8 Hz, 2H), 6.29 (br s, 2H), 7.36 (dd, J = 1.2, 8.4 Hz, 1H), 7.63 (s, 1H), 7.87 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.5, 150.4, 138.4, 131.9, 130.6, 120.2, 119.6, 113.6, 62.2, 20.8, 14.3; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{11}H_{13}N_3NaO_2$ 242.0906, found 242.0902.

*Ethyl 3,5-diamino-1H-indazole-1-carboxylate (**10j**):* yellow solid, 82 mg, 75% yield; mp 181−182 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.33 (t, J = 7.2 Hz, 3H), 4.31 (q, J = 7.2 Hz, 2H), 5.09 (br s, 2H), 6.07 (s, 2H), 6.82−6.84 (m, 2H), 7.67 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.5, 150.3, 144.8, 132.6, 120.5, 118.1, 114.4, 102.4, 61.8, 14.4; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{10}H_{12}N_4NaO_2$ 243.0858, found 243.0852.

*Ethyl 3-amino-5-bromo-1H-indazole-1-carboxylate (**10k**):* yellow solid, 59 mg, 42% yield; mp 136−138 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.36 (t, J = 7.2 Hz, 3H), 4.35 (q, J = 7.2 Hz, 2H), 6.45 (br s, 2H), 7.66−7.69 (m, 1H), 7.94 (d, J = 8.8 Hz, 1H), 8.14 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.8, 150.2, 139.8, 131.8, 123.4, 121.1, 115.8, 114.6, 62.7, 14.2; HRMS (ESI-FT) m/z (M + Na)$^+$ calcd for $C_{10}H_{10}BrN_3NaO_2$ 305.9854, found 305.9850.

General Procedure for Preparing 1-Aryl-3-aminoindazoles. A Schlenk tube was charged with 2-iodobenzonitrile (0.5 mmol), N′-phenylbenzohydrazide (0.60 mmol), CuBr (0.05 mmol), *trans*-4-hydroxy-L-proline (0.1 mmol), and K_2CO_3 (2.0 mmol). The tube was evacuated and backfilled with argon before 1.5 mL of DMSO and 0.15 mL of H_2O were added. After the reaction mixture was stirred at 90 °C for 36−48 h, 10 mL of saturated NH_4Cl solution was added at room temperature to quench the reaction. The mixture was extracted with EtOAc, and then the organic layer was washed with water and brine and dried over Na_2SO_4. After concentration in vacuo, the residue was purified by column chromatography (eluting with Et_3N/EtOAc/hexane) to provide the desired product.

*1-Phenyl-1H-indazol-3-amine (**10l**):* yellow solid, 85 mg, 82% yield; mp 87−89 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.93 (s, 2H), 7.09 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.2 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.8, 140.7, 138.7, 129.3 (2C), 127.9, 123.8, 119.8 (2C), 119.4, 117.3, 109.9; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{13}H_{12}N_3$ 210.1031, found 210.1025.

*6-Methyl-1-phenyl-1H-indazol-3-amine (**10m**):* yellow solid, 81 mg, 73% yield; mp 121−123 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.43 (s, 3H), 5.85 (s, 2H), 6.92 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.2 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.54 (s, 1H), 7.68 (d, J = 8.4 Hz, 2H), 7.73 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.7, 140.8, 139.4, 137.8, 129.3 (2C), 123.7, 121.3, 120.7, 119.9 (2C), 115.5, 109.6, 21.7; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3$ 224.1188, found 224.1182.

*5-Methyl-1-phenyl-1H-indazol-3-ylamine (**10n**):* semisolid, 82 mg, 72% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.39 (s, 2H), 5.81 (s, 1H), 7.15 (t, J = 7.3 Hz, 1H), 7.24 (d, J = 9.5 Hz, 1H), 7.46 (t, J = 7.9 Hz, 2H), 7.67−7.63 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.4, 140.9, 137.4, 129.6, 129.3 (2C), 128.3, 123.5, 120.3, 119.4 (2C), 117.6, 109.9, 20.8; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3$ 224.1188, found 224.1182.

*5-Methoxy-1-phenyl-1H-indazol-3-ylamine (**10o**):* semisolid, 89 mg, 75% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.80 (s, 3H), 5.79 (br s, 2H), 7.06 (dd, J = 9.1, 2.5 Hz, 1H), 7.14 (t, J = 7.4 Hz, 1H), 7.39 (d, J = 2.6 Hz, 1H), 7.45 (t, J = 7.9 Hz, 2H), 7.69−7.63 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.3, 150.4, 140.9, 134.5, 129.3 (2C), 123.4, 119.2 (2C), 118.5, 117.5, 111.2, 101.7, 55.5; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3O$ 240.1137, found 240.1131.

*5-Fluoro-1-phenyl-1H-indazol-3-amine (**10p**):* yellow solid, 78 mg, 69% yield; mp 108−110 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.93 (br s, 2H), 7.19 (t, J = 7.2 Hz, 1H), 7.28 (dt, J = 7.2, 2.4 Hz, 1H), 7.47 (t, J = 8.0 Hz, 2H), 7.67 (d, J = 8.8 Hz, 3H), 7.76 (dd, J = 9.2, 4.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.3 (J = 233.6 Hz), 150.6 (J = 4.7 Hz), 140.4, 135.9, 129.4 (2C), 124.1, 119.8 (2C), 117.1 (J = 9.5 Hz), 116.7 (J = 26.4 Hz), 111.5 (J = 9.1 Hz), 105.6 (J = 23.6 Hz); HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{13}H_{11}FN_3$ 228.0937, found 228.0932.

*1-(4-Methoxyphenyl)-1H-indazol-3-amine (**10q**):* semisolid, 84 mg, 71% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.79 (s, 3H), 5.80 (br s, 2H), 7.03−7.06 (m, 3H), 7.34−7.38 (m, 1H), 7.54−7.59 (m, 3H), 7.83−7.81 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.1, 150.3, 138.8, 133.9, 127.5, 121.9 (2C), 120.9, 118.8, 116.5, 114.5 (2C), 109.4, 55.3; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3O$ 240.1137, found 240.1131.

*1-(4-Bromophenyl)-1H-indazol-3-amine (**10r**):* semisolid, 99 mg, 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20 (br s, 2H), 7.15−7.11 (m, 1H), 7.25−7.23 (m, 1H), 7.38−7.43 (m, 1H),7.46−7.50 (m, 2H), 7.62 (d, J = 7.6 Hz, 1H), 7.69−7.66 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 140.6, 139.9, 129.50 (2C), 128.1, 125.3, 121.6 (2C), 120.1, 119.8, 116.7, 110.5; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{13}H_{11}BrN_3$ 288.0136, found 288.0131.

*1-p-Tolyl-1H-indazol-3-amine (**10s**):* white solid, 82 mg, 74% yield; mp 112−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3H), 4.20 (br s, 2H), 7.12 (t, J = 7.6 Hz, 1H), 7.28−7.25 (m, 2H), 7.40−7.36 (m, 1H), 7.54−7.52 (m, 2H), 7.63−7.59 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 139.8, 138.1, 134.9, 129.9 (2C), 127.8, 121.6 (2C), 119.8, 119.7, 116.4, 110.3, 21.0; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3$ 224.1188, found 224.1182.

*1-(4-Fluorophenyl)-1H-indazol-3-amine (**10t**):* semisolid, 79 mg, 70% yield; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.05 (br s, 2H), 6.97−7.01 (m, 1H), 7.12−7.16 (m, 1H), 7.42−7.58 (m, 4H), 7.82 (d, J = 8.8 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.9 (J = 241.4 Hz), 151.2, 142.4 (J = 10.8 Hz), 138.8, 131.1 (J = 9.6 Hz), 128.3, 121.2, 120.0, 117.8, 115.0 (J = 2.6 Hz), 110.3, 110.2 (J = 21.0 Hz), 106.5 (J = 25.6 Hz); HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{13}H_{11}FN_3$ 228.0937, found 228.0932.

*1-(3-Methoxyphenyl)-1H-indazol-3-amine (**10u**):* semisolid, 78 mg, 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (s, 3H), 4.16 (br s, 2H), 6.77−6.80 (m, 1H), 7.12 (t, J = 8.0 Hz, 1H), 7.26−7.23 (m, 2H), 7.34−7.39 (m, 2H), 7.59 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 149.2, 141.7, 139.8, 130.1, 127.9, 120.1, 119.8, 116.8, 113.6, 111.1, 110.6, 107.3, 55.5; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3O$ 240.1137, found 240.1131.

*1-(3-Chlorophenyl)-1H-indazol-3-amine (**10v**):* yellow solid, 80 mg, 66% yield; mp 102−105 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26 (br s, 2H), 7.20−7.14 (m, 2H), 7.46−7.37 (m, 2H), 7.62−7.57 (m, 2H), 7.71−7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 141.7, 139.6, 134.9, 130.3, 128.2, 124.7, 121.1, 120.4, 119.9, 118.8, 117.1, 110.3; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{13}H_{11}ClN_3$ 244.0642, found 244.0636.

*1-o-Tolyl-1H-indazol-3-amine (**10w**):* semisolid, 66 mg, 60% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.17 (s, 3H), 4.19 (br s, 2H), 7.00−7.04 (m, 2H), 7.22−7.33 (m, 5H), 7.56 (d, J = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.5, 141.7, 138.5, 135.7, 131.4, 128.1, 127.5, 127.5, 126.7, 119.6, 119.4, 115.3, 110.1, 18.2; HRMS (ESI-FT) m/z (M + H)$^+$ calcd for $C_{14}H_{14}N_3$ 224.1188, found 224.1182.

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra for all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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